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Late Recurrence of Clear Cell Sarcoma of the Kidney

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Clear cell sarcoma of the kidney (CCSK) is a rare pediatric neoplasm with particular propensity for bone metastasis that requires aggressive therapy. We report a patient with CCSK who was misreported as having Wilm's tumour at the time of initial diagnosis and received only minimal therapy. The disease recurred locally after 8 years, with no evidence of distant metastasis. Important clinical and histologic features of CCSK are described, along with a review of the literature. Med. Pediatr. Oncol. 28: 355–357, 1997

Key words: clear cell sarcoma; kidney; late recurrence

INTRODUCTION

Clear cell sarcoma of the kidney (CCSK) is a rare neoplasm accounting for less than 4% of childhood renal tumors. It was recognised as a neoplasm distinct from Wilm's tumor by Kidd in 1970, by virtue of its propensity to metastasize to bones [1]. Marsden and Lawler noted osseous metastases in 60% of patients with renal clear cell sarcoma and coined the term ''bone metastasizing renal tumour'' [2]. It is important for pathologists to be familiar with the histologic appearance of this highly malignant tumour so they can provide an accurate diagnosis. We report a patient who was misdiagnosed and treated as having Wilm's tumour, with minimal chemotherapy. The disease recurred locally 8 years after therapy without any evidence of distant metastasis. We report this unusual clinical behaviour of CCSK and provide a review of the literature on the natural history and pathologic features of this tumour.

CASE REPORT

A 4-year-old boy was admitted to the pediatric surgery ward of S.A.T. Hospital in August 1982 with complaints of pain and abdominal distension of 1 month's duration. He had no associated vomiting, diarrhea, constipation, or hematuria. His height and weight were 94 cm and 12 kg, respectively, and his general condition was unremarkable. Abdominal examination revealed a large mass in the left lumbar area, clinically suggestive of a renal swelling. Other systems were within normal limits. Laboratory investigations such as complete blood counts, liver and renal function tests, and chest radiographs were normal. Intravenous urography demonstrated displacement and distortion of renal calyces on the left side and a normal right kidney. A clinical diagnosis of Wilm's tumor was made. At laparotomy, the right kidney, liver, and para-aortic area were normal and the left kidney showed a well-encapsulated mass at its lower pole. A left-sided nephroureterectomy was done without operative spillage.

Gross examination of the nephrectomy specimen showed a well-defined, creamy-white, fleshy neoplasm 15 × 10 × 8 cm in size, with areas of necrosis and hemorrhage on cut section. On microscopy, there were loosely arranged short and spindle-shaped cells with bland appearance. Areas of necrosis and hemorrhage were seen in some sections. No definite triphasic pattern or tubular differentiation was seen, and a diagnosis of monophasic, purely blastemal type of nephroblastoma was made. There was no evidence of breach of tumour capsule. The patient was considered as having favourable histology Stage I Wilm's tumor and was treated with combination chemotherapy, using vincristine (VCR) and actinomycin D (AMD).

The patient participated in regular follow-up and maintained a disease-free status until December 1990, when he presented with a history of an abdominal mass of 2 weeks' duration. Clinically, there was a firm and nontender mass occupying the left lumbar and hypochondrial areas. The mass was well defined and showed irregular echotexture on ultrasonography. Other investigations did not reveal evidence of disease elsewhere. Laparotomy revealed a recurrent nodular mass 25 × 25 cm in

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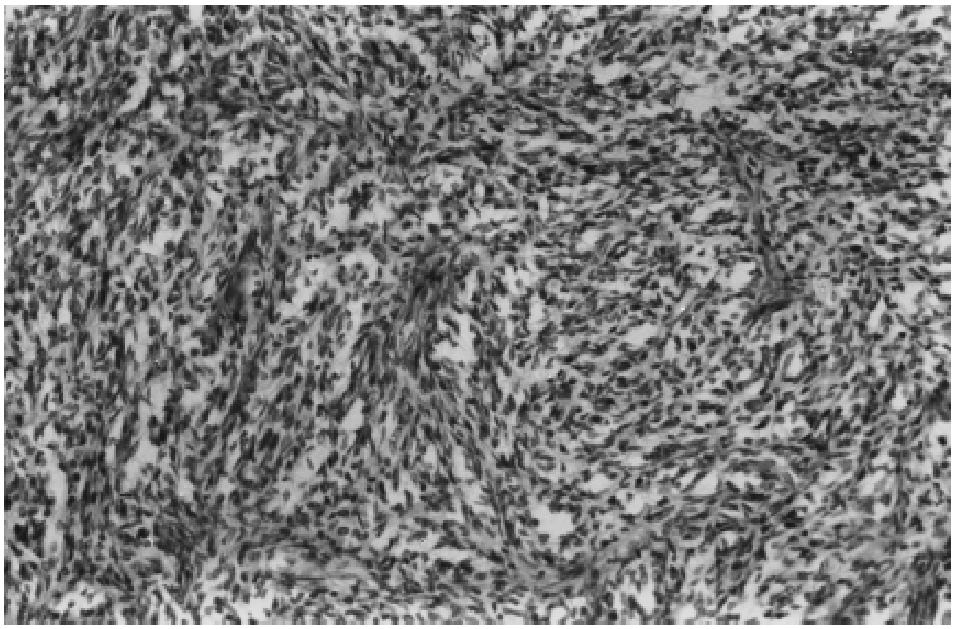

Fig. 1. Photomicrograph showing neoplasm composed of spindle or ovoid cells with scanty vacuolated cytoplasm, arranged loosely. H&E, × 450.

size extending superiorly behind the pancreatic bed and inferiorly to the pelvic brim. The mass was found crossing the midline and surrounding the aorta. Excision of the mass was difficult, and only a debulking surgery was done.

Histologically, the neoplasm showed a monomorphic appearance with moderate and highly cellular areas. The neoplastic cells were arranged in sheets, with the cells showing round or ovoid nuclei and poorly stained cytoplasm with indistinct outline. The stroma showed fibrovascular appearance with fine capillaries. Stromal myxoid change was also noted. Cystic spaces with eosinophilic material were seen in some areas along with necrosis and hemorrhage (Fig. 1). The appearance was consistent with CCSK. A subsequent review of previous slides also revealed features consistent with clear cell sarcoma. Metastatic work-up, including skeletal survey and bone scan, was negative. Salvage therapy was attempted with combination chemotherapy and local radiotherapy. Response to treatment was poor, and the patient died of progressive local disease after 4 months.

DISCUSSION

CCSK is a malignant renal tumor of childhood with a very aggressive natural history. As an entity, CCSK was first recognised by Kidd in 1970 when he reviewed seven ''sarcomas of the kidney with predisposition to metastasize to bone'' [1]. Subsequently Marsden and Lawler described a few cases of bone metastasizing renal tumors in childhood [2]. The same tumor was described as clear cell sarcoma based on clear cytoplasm of the tumor by Beckwith and Palmer [3].

The incidence of CCSK among primary tumors of childhood has been variously reported. The values range from 1.6% in Marsden and Lawler's series to 4.06% as reported by Sotelo-Avila et al. [4]. A total of 120 cases of CCSK were identified among 2,841 renal neoplasm entered in the National Wilms Tumor Study Group (NWTSG) I, II, and III, with a frequency of 4.2% [5]. Chellam et al. reported a frequency of 3.7% [6]. The age at presentation was similar to that seen in Wilm's tumor [7]. The striking male predominance reported by Marsden and Lawler (7.6:1) was not observed by Sotelo-Avila et al. (1.3:1) or the NWTSG (1.5:1) [2,4,5].

On gross examination, the bulging cut surface of CCSK is uniform, lobular, and grey-white or variegated, from firm grey-white whorled areas to soft, fleshy pink-white tissue, separated by broad bands of necrosis. Hemorrhage is uncommon. Some tumors produce abundant mucinous material that imparts a glistening appearance to the cut surface.

Beckwith [7] described the classic and variant patterns of CCSK. In the classic pattern, the neoplasm is composed of tumor cells in nests or cords separated by an evenly distributed arborising network of blood vessels supported by a spindle cell stroma. The vascular pattern is highlighted in reticulin preparations, and this aids in diagnosis. Epithelioid trabecular pattern, neurilemoma-like nuclear pallisading, fibrosis with stromal hyalinisation, and myxoid and cystic patterns are also described.

Careful examination of vascular pattern, tumor edge,

and nuclear detail may be helpful in distinguishing CCSK from other renal tumors of childhood. In our patient, histologic diagnosis of CCSK was not established at the first instance because our pathologists were unfamiliar with this entity at that time.

Histogenesis of the tumor remains enigmatic. Ultrastructurally, tumor cells of CCSK suggest mesodermal derivation, but it has been impossible to trace the histogenesis of the tumor to any specific cell type. Because CCSK appears to arise from renal medulla, the renomedullary interstitial cell (RMIC) was proposed as the precursor by Beckwith [7]. However, ultrastructurally, neoplastic cells in CCSK are quite different from RMIC [8,9]. Fibroblasts, smooth muscle cells, pericytes, Schwann cells, and blastemal cap cells are also considered in the histogenesis of CCSK.

On the basis of histologic, ultrastructural, and clinical characteristics, CCSK should not be considered a variant of Wilm's tumor. Extrarenal clear cell sarcomas have not been reported. Other clear cell tumors, like those of tendo-aponeurosis and thymus, and mesonephric carcinoma containing clear cells are histologically and ultrastructurally different from CCSK.

The reported frequency of bone metastasis in CCSK varies widely. In a series of 38 patients with CCSK reported by Marsden and Lawler, bone metastases developed in 29 patients (76%), with a 86% 5-year mortality rate [2]. NWTSG reported bone metastases, with or without other sites, in 17 of 36 patients at the time of first relapse [5]. Bone metastasis occurred in 12 of 21 patients in the series reported by Sotelo-Avila et al. In this series, bone metastasis heralded the development of metastatic disease at other sites in nine patients [4]. Polyostotic metastatic involvement was also documented [4]. The pattern of metastasis is not apparently altered by chemotherapy or radiotherapy. The possible role of prostaglandins in the development of skeletal metastasis by CCSK, as suggested in sarcomatous Wilm's tumour, is being investigated [10].

Despite its high metastatic potential, there is evidence to suggest that local radiotherapy and aggressive chemotherapy may be beneficial in the treatment of CCSK [5,11]. The addition of doxorubicin (DOX) to the combination of VCR and AMD appeared to improve relapse-free survival, as reported by the NWTSG [5]. The 6-year relapse-free survival rate for children treated with VCR, AMD, and radiation was 25% compared with 63.5% for children treated with VCR, AMD, DOX, and radiation. However, addition of cyclophosphamide (CTX) did not improve the relapse-free survival rate [5]. It is possible that CTX used in a higher dose intensity may show increased therapeutic efficacy, as evidenced by the activity of a combination of ifosfamide and etoposide on CCSK [5,12].

Children with CCSK are at risk of late disease recurrence. The NWTSG reports improved relapse-free survival at 6 years to account indirectly for late failures [5]. Thirty percent of relapses occurred more than 2 years after diagnosis, and children with CCSK must be monitored for a prolonged period before the risk of recurrence becomes negligible [5].

CONCLUSION

The long disease-free interval of 8 years after minimal chemotherapy and absence of skeletal metastasis at the time of local recurrence makes our case unique in its natural history. It is important that pathologists familiarise themselves with this entity, so that correct histologic diagnoses can be made and intensive treatment attempted. Children with CCSK need longer follow-up periods with more frequent intervals for detection and treatment of relapses.

REFERENCES

1. Kidd JM: Exclusion of certain renal neoplasms from the category of Wilm's tumor. Am J Pathol 57:164, 1970.
2. Marsden HB, Lawler W: Bone metastasizing renal tumor of childhood. Histopathological and clinical review of 38 cases. Virchows Arch A 387:341–351, 1980.
3. Beckwith JB, Palmer NF: Histopathology and prognosis of Wilm's tumor. Results from the first National Wilm's Tumor Study. Cancer 41:1937–1948, 1978.
4. Sotelo-Avila C, Gonzalez Crussi F, Sadowinski, Gooch WM, Pena R: Clear cell sarcoma of kidney. A clinicophatological study of 21 patients with long term follow up evaluation. Hum Pathol 16:1219–1230, 1986.
5. Green DM, Breslow NE, Beckwith JB, Moksness J, Finklestein JZ, D'Angio GJ: Treatment of children with clear-cell sarcoma of the kidney: A report from the National Wilms Tumor Study Group. J Clin Oncol 12(10):2132–2137, 1994.
6. Chellam VG, Chacko E, Kusumakumary P, Surendran N: Clear cell sarcoma of kidney. A clinicopathological study of 4 cases. Indian J Cancer 26:120–128, 1989.
7. Beckwith JB: Wilm's tumor and other renal tumours of childhood: A selective review from the National Wilm's Tumor Study Pathology Centre. Hum Pathol 14:481–492, 1983.
8. Gonzalez-Crussi F, Baum ES: Renal sarcoma of childhood—A clinicopathological and ultrastructural study. Cancer 51:898–912, 1983.
9. Hass JE, Bonadio JF, Beckwith JB: Clear cell sarcoma of kidney with emphasis on ultrastructural studies. Cancer 54:2978–2987, 1984.
10. Calo L, Cantaro S, Bertuzzo L, Vianello A, Vido L, Borasatti A: Synthesis and catabolism of PGE_2 by a nephroblastoma associated with hypercalcaenia without bone metastasis. Cancer 54:635–637, 1984.
11. Beckwith JB, Larson E: Clear cell sarcoma of kidney. Pediatr Pathol 9:211–218, 1989.
12. Green D, Beckwith J, Breslow N. The treatment of children with focal or diffuse anaplastic Wilm's tumor. A report from the National Wilm's Tumor Study. Proc Am Soc Clin Oncol 13:413, 1994.